Attachment 1.

Date 19/8/85

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. A.M. Molla — Trainee Investigator (if any) _____

Application No. 85-019 — Supporting Agency (if Non-ICDDR,B) _____

Title of Study "Comparison of efficacy & digestibility of Plantain-salt & Rice-salt as home fluid with standard Glucose ORS in the management of dehydration in acute diarrhoea in children."

Project status:
( ) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects — (Yes) No
   (b) Non-ill subjects — Yes (No)
   (c) Minors or persons under guardianship — (Yes) No
2. Does the study involve:
   (a) Physical risks to the subjects — Yes (No)
   (b) Social Risks — Yes (No)
   (c) Psychological risks to subjects — Yes (No)
   (d) Discomfort to subjects — Yes (No)
   (e) Invasion of privacy — Yes (No)
   (f) Disclosure of information damaging to subject or others — Yes (No)
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other) — (Yes) No
   (b) Use of fetal tissue or abortus — Yes (No)
   (c) Use of organs or body fluids — (Yes) No
4. Are subjects clearly informed about:
   (a) Nature and purposes of study — (Yes) No
   (b) Procedures to be followed including alternatives used — (Yes) No
   (c) Physical risks — Yes (No)
   (d) Sensitive questions — Yes (No)
   (e) Benefits to be derived — (Yes) No
   (f) Right to refuse to participate or to withdraw from study — (Yes) No
   (g) Confidential handling of data — (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — (Yes) No
5. Will signed consent form be required:
   (a) From subjects — Yes No
   (b) From parent or guardian (if subjects are minors) — (Yes) No
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
   ___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   NA Informed consent form for subjects
   ✓ Informed consent form for parent or guardian
   ✓ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. Description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

(PTO)

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

A. Molla
Principal Investigator

Trainee

85-019
19/8/85

SECTION I : RESEARCH PROTOCOL

1.	TITLE	:	Comparison of efficacy and digestibility of Plantain-salt and Rice-salt as home fluid with standard Glucose ORS in the management of dehydration in acute diarrhoea in children.
2.	PRINCIPAL INVESTIGATOR	:	Dr. A. M. Molla
	CO-INVESTIGATORS	:	Dr. Asma Khanam Dr. Ayesha Molla One Physician (to be named)
	CONSULTANTS	:	Dr. R. Eeckels Dr. W.B. Greenough III
3.	STARTING DATE	:	1 month after approval by RRC and ERC of ICDDR,B.
4.	COMPLETION DATE	:	1 year after starting.
5.	TOTAL DIRECT COST	:	US DOLLARS 31,691.00
	AVAILABILITY OF FUND	:	To be submitted to donor agency.
6.	SCIENTIFIC PROGRAMME	:	This protocol has been approved by Pathogenesis and Therapy Working Group.

Signature of the Head, Pathogenesis and Therapy Working Group

7. ABSTRACT SUMMARY:

The superiority of rice-based oral rehydration solution (ORS) over the standard glucose-based WHO/UNICEF ORS in terms of acceptability, calorie supplementation, reduction in stool output and vomiting has already been established in ICDDR,B. However, rice is not the only staple in different parts of the world. Many other cereals like maize, millet, sorghum, wheat, and also casava, sago, potato etc. are used as staple by a substantial proportion of the world's population. Similarly, plantains are used as staple by large proportion of the total world population. One clinical trial with plantain-salt solution and maize ORS is ongoing in Dar-es-salam, Tanzania. Because of lack of facilities, Tanzanian study would not be able to go into indepth investigations to evaluate the digestibility of the plantain based ORS. Therefore, it is proposed to study both the efficacy and digestibility of plantain-salt-solution and rice-salt-solution. A total of 150 children of age between 1 month and 59 months with history of 48 hours diarrhoea having mild to moderate degree of dehydration will be studied in the clinical research unit of ICDDR,B. 50 patients will be assigned to each of rice-salt and plantain-salt solution and 50 others will be studied as control who will be treated by standard glucose-based WHO/UNICEF ORS. Out of the 50 patients, 40 will be studied for efficacy part and 10 patients will be assigned to the digestibility part in both rice and plantain based ORS. Efficacy will be determined on the basis of ORS consumption, stool and urine output, vomitus, serum specific gravity, gain in body weight and correction and maintenance of electrolytes. Digestibility will be determined by the glucose in the stool before and after hydrolysis of plantain and rice

salt solutions, pH and osmolality.

8. REVIEWS:

(a) Ethical Review Committee: _____

(b) Research Review Committee: _____

(c) Director, ICDDR,B: _____

SECTION II : RESEARCH PLAN

A. INTRODUCTION:

1. OBJECTIVES OF THE STUDY:

The aim of this study is to evaluate the relative efficacy of plantain-salt and rice-salt solutions and compare them with that of standard WHO/UNICEF glucose ORS in children with acute diarrhoea. Besides, this protocol also aims at studying the digestibility of rice-salt and plantain-salt solution in a small number of young children using metabolic balance techniques.

2. BACKGROUND:

Diarrhoea is one of the major health hazards to children in the developing as well as in the developed countries. It is amongst the first five important causes of mortality in children in the developing world. The efficacy of oral rehydration therapy in replacing the loss of fluid and electrolytes in watery diarrhoea has been well established (1-4). Oral rehydration therapy has in recent years reduced the mortality due to diarrhoea and has diminished the need of I.V. fluid therapy except in most severe cases. The discovery of glucose facilitated transport of sodium and water in the small intestine led to the use of glucose electrolytes solution for effective therapy of dehydration in acute watery diarrhoea (5). The ORT at the same time is reasonably cheaper and acceptable by the patient. Since glucose is not universally

available and expensive in some countries, it was replaced by sugar (6). In further simplification Gur and Molasses has been used in place of sugar (7). Recently the cereal (rice powder) has been used with improved results (8,9). The results of rice-based ORS (8,9) using 50 g or two fistful of rice flour has shown to reduce (i) stool output and ORS intake by 40-50% (10), (ii) vomiting by 60% and (iii) compared to the glucose ORS, rice ORS contains 1½ times more calories and rehydrates more efficiently as shown by gain in body weight and change in serum specific gravity. It is effective in correcting biochemical abnormalities and maintaining them within normal limit.

Plantain or green banana is grown very widely in the tropical region all over the world including Bangladesh. In many of the African, Caribbean, Central and South American countries it is extensively used as a staple diet (11) as well as a fruit. Hence the plantain is not only highly valued as food but also readily available in these countries.

Traditionally plantain is used as a recovery diet in debilitated and recovering patients as well as a diarrhoea therapy in Bangladesh and many developing and developed countries.

Plantain-salt rehydration fluid may have manifold advantages compared to glucose/sucrose ORS.

1. Being a food, it will be readily acceptable in the plantain growing countries.
2. It is readily available all the year round.
3. Relatively cheap.

4. Being available at home, it would eliminate the storage and transport of ORS packets - attaining a certain level of self-sufficiency.
5. Assuming that the plantain starch, like other starches is being digested by intraluminal enzymes, its glucose molecules should be liberated slowly into the intestinal lumen and at the mucosal surface (12).
6. And for the same reason the starch would not cause rise of osmolality inside the intestinal lumen.

Therefore, a higher amount of carbohydrate could be used in the rehydration solution to provide more calories.

Plantain contains sufficient potassium and some antidiarrhoeal elements like pectin and lignin, making it a potential diarrhoea therapy (13-14). Because of its high content of indigenous potassium, plantain with added salt will possibly allow to make an excellent home-made rehydration fluid. Similarly, rice-salt solution can also make another effective home-made fluid. However, it is essential to conduct a clinical trial with both of these kinds of ORS before they are taken to the field.

Preparation of the plantain-salt solution involves boiling the plantain in water intact with skin for 10-15 minutes. The skin will be peeled off, mashed and mixed with water, forming a homogenous solution. This requires time and fuel, but it should be seen in the light of the advantages of food based rehydration therapy. In any case, in plantain eating countries, plantain is always cooked before consumption. The water once used for the cooking can also be used for

making the plantain-salt solution. Therefore, boiling the plantain for the preparation of rehydration fluid would not be considered a hindrance. The boiling of both plantain and rice is necessary to soften it, to hydrate the starch (15) and ease the hydrolysis of disaccharides which is completed at the mucosal surface. Unhydrolysed polysaccharides reaching the colon often interact with bacteria producing degradation products causing fluid secretion, increased motility, cramps, irritation and distension. Hence full hydration of starch by boiling will help hydrolysis and release glucose molecules easily.

CRITERIA FOR SELECTING POSSIBLE CEREALS/FOOD FOR CLINICAL TRIAL:

In order to qualify for being used in ORS/home fluid, the staple food concerned must be:

1. Available and cheap;
2. Easily digestible;
3. Easy to prepare;
4. Acceptable by the concerned population;
5. Used by a large number of population as staple food;
6. Have a satisfactory biochemical composition;
7. Free from side affects.

Both rice and plantain qualify according to the above criteria.

COMPOSITION OF DIFFERENT CEREALS TO BE USED FOR TRIAL:

Table 1 compares the composition of the ripe banana and rice. But ripe banana cannot be used in rehydration fluid because it decomposes within two hours. Plantain is more suitable from that point.

Rice and plantain have adequate carbohydrate and in right proportion and should be good glucose substitute in the rehydration solution. Plantain based ORS was tested in a preliminary study for its acceptibility, by 10 doctors of the ICDDR,B and 20 OPD patients. All of them accepted it well. In vitro, hydrolysis carried out in ICDDR,B showed the glucose content of rice to be 80 per 100g of dry rice and 16.4 per 100g of plantain. The plantain has high content of potassium as compared to any cereal. Lebenthal et al (12) showed that 85% of young children (12 months) recovering from acute diarrhoea can tolerate and absorb glucose from corn syrup. Evidence exists that plantain was used for nutritional management of premature infants. These information indicate that plantain has the theoretical qualification for preparing a rehydration fluid. The biochemical composition of cooked plantain as carried out in ICDDR,B is presented in Table II. Based on the glucose content of different cereals, the composition of one litre of the proposed rehydration fluid is shown in Table III.

3. RATIONALE:

(a) Rice powder ORS has been shown to be superior to WHO/UNICEF glucose ORS. Plantain being a major staple food in many countries, it is desirable to use it in a clinical trial to study the efficacy of plantain based ORS for rehydration during acute diarrhoea.

(b) Because of its composition, plantain could be effectively used to replace the glucose in home-made rehydration fluid.

(c) Plantain has a high potassium content and it will eliminate the need for adding potassium to the rehydration fluid. Therefore, the plantain-salt-solution will have adequate potassium content

which is so appropriate in the developing country where both hypokalaemia and malnutrition are present. Thus an inexpensive and superior home-made fluid will be made available to the target population. Traditionally in many African, Asian and also other plantain eating countries, plantain is used as dietary therapy during diarrhoea and after recovery. Therefore, the proposed rehydration solution will be an acceptable rehydration fluid and it will possibly increase the users' rate of ORT in the countries concerned.

(d) Before widely recommending plantain-salt-solution, it is essential to test its efficacy in a well controlled set-up in the developing countries where it is a staple food for a large number of people.

(e) Rice-based ORS with complete electrolyte formula has been found superior to glucose-based ORS. But rice-based rehydration solution at home should be rice-salt-solution. This has not been given a trial in a clinical set-up and hence it is essential to conduct this trial in order to see its efficacy compared to other rehydration fluids.

(f) Thus if found successful, two home-made fluid will be available for immediate application to the appropriate countries.

B. SPECIFIC AIMS:

1. To study the digestibility of plantain-salt and rice-salt solution as reflected by pH, osmolality and the glucose content in the stool before and after acid hydrolysis.

2. To study the efficacy of different rehydration solutions made from plantain and rice in terms of the stool output, ORS consumption, vomiting, electrolyte balance, body weight gain, and duration of

diarrhoea.

3. To compare all the above variables with standard glucose-based ORS.

C. METHODS AND PROCEDURES:

1. Preparation and composition of the different oral rehydration solutions to be used in the study.

(a) Plantain-salt-solution*

Two plantain banans (approximately 200 g) will be boiled with the intact skin in about 1½ litre of water for about 15 minutes. The skin will then be peeled off and the plantain bananas will be mashed and mixed in 1 litre of the already boiled water. 5.0 g of salt will be added; the solution will be thoroughly mixed, and served to the patients.

(b) Rice-salt-solution*

50 g rice powder will be added to 1100 ml of water, boiled for 6-7 minutes while stirring continuously. Once a smooth mixture is obtained, 5.3 g salt will be added, mixed and the preparation served to the patients.

(c) Glucose-ORS

Prepared packets will be dissolved in one litre of water.

2. Selection of the patients

This study will be carried out in the study ward and metabolic unit of

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*According to WHO laid principles, rehydration media containing complete formula is termed as ORS. Any rehydration media with incomplete formula is called rehydration solution.

ICDDR,B. Patients will be selected according to the following criteria:

(a) Diarrhoea will be defined as three or more liquid stool in 24 hours.

(b) Table IV presents the criteria for selection of patients.

The study aims at finding the efficacy and digestibility of the plantain-salt and rice-salt solutions. The efficacy part will be studied in all qualifying children group up to 5 years and the digestibility will be tested only in children of age between 1-6 months. The inclusion criteria initially will depend mainly on clinical diagnosis as the microbiological confirmation will not be available within next 24 hours. Therefore clinically suspected cases of cholera, ETEC and rotavirus diarrhoea will be admitted and randomly assigned to the study group. Stool microscopy and dark field microscopy results will be available within 2-3 hours of admission. Any patient not fulfilling the criteria as laid down in Table IV will be excluded. As this protocol is going to test the efficacy of home-made solutions patients with mild and moderate dehydration will be included. Because of difficulty in collecting urine bags will be used for collection of urine. Any patients showing signs of systemic illness or signs of invasive diarrhoea (pus cells 20 HPF) will be excluded. The procedure of the study will be fully explained to the parents and informed consent will be obtained before initiating the study. Antibiotics will be withheld till the study is over and anyone needing antibiotic on clinical grounds will be taken out of the study.

3. SAMPLE SIZE

The sample size n for each study group is usually determined as follows:

$$n = \left(\frac{\sigma}{d}\right)^2 f(\alpha,\beta)$$

Where σ is the standard deviation of the difference of two group means and d is the minimum difference between two means which will be detected as significant by a test procedure at a level of significance $\alpha = .05$. The power of the test is $1-\beta = .95$, $\alpha = .05 = \beta$ f $(\alpha,\beta) = 13.0$. Although it is expected that cereal based ORT will reduce stool output by 30%, we have no idea about the value of σ. In the absence of any idea about σ we assumed that the ratio σ/d should under no circumstances exceed 2 which when put into the formula of n above (with $f(\alpha,\beta) = 13$), n becomes equal to 52. This means that we need about 156 patients to measure the efficacy of the three types of ORT solutions. It is to be noted that with this much sample size nonparametric tests such as Median test or Kruskar-Wallis test could also be used to test the significance of the three groups of ORT solution.

4. RANDOMIZATION PROCEDURE

The study will be randomized but cannot be blinded because of the distinctive colour and consistency of the solutions. A random table will be prepared with same numbers of patients for each of the food-based solution and control ORS. Then a small ticket for each patient will be made and inserted into a box. When a patient is admitted, the nurse on duty will pick up one ticket from the box and assign the patient to the study group accordingly. Since there will not be an observation period

before starting the study, stratified randomization is not possible.

5. COMPARABILITY OF THE STUDY PATIENTS

Study patients will be selected according to the laid down criteria. Since this protocol will only accept patients with mild and moderate dehydration as may exist in the community, they will be directly assigned to the different rehydration therapy group. Therefore a period of observation (8 hours),during which time rate of purging could be observed, will not be possible. However, a table (No. V) is provided showing the comparability in a previous study. During selection, attention will be paid to select patients with similar criteria.

6. LABORATORY INVESTIGATIONS ON ADMISSION AND AT 24 HOURS

Laboratory investigations will include total and differential white blood count, haematocrit, serum specific gravity and electrolytes, urine for routine microscopy and stool for microscopic analysis for pus cells, ova, cysts or parasites. Liquid stool and rectal swab will be sent for culture in all plates. Rectal swabs from each patient will be saved in deep freeze for ELISA test for rotavirus. E. coli isolates will be tested for ST and LT toxins.

7. INITIAL CLINICAL PROCEDURES

On admission into the study, assessment of dehydration and a thorough clinical examination of each patient will be carried out by one of the investigators. Height or length and weight will be taken in a paediatric scale accurately up to 1 g. Since the patients with severe dehydration will not be included all patients will receive the assigned oral

rehydration solution from the beginning. The initial rehydration will be done with the required volume calculated on the basis of body weight following WHO guidelines. The required amount of fluid will be fed within 4 hours of admission. Any stool output during this time will be replaced by rehydration fluid. In case the patient is alert and willing to take breast milk, feeding will be allowed even before the completion of initial rehydration. For non-breast fed patients usual hospital diet will be given after the completion of initial rehydration on demand even before. The efficacy study will be continued until the patient stops passing luquid stool up to a maximum of 5 days. Any child passing watery stool more than 5 days will be declared as clinical failure and will be investigated further.

During the study period the following data will be collected:

a. Weight and height on admission;

b. Vital signs like pulse, respiration and BP every 8 hour;

c. Weight every day;

d. Clinical assessment of hydration state 8 hourly;

e. Blood for Hct, Ser. specific gravity, electrolytes on admission and at 24 hours;

f. Accurate measurement of stool, urine, vomit output and intake of food and fluid every 8 hour.

Required amount of rehydration fluid will be measured accuratley and given to the mother or attendants to feed the patients under close supervision of the study nurse. Measured quantity of plain water will be allowed to each child. Clinical evaluation of skin elasticity, mucous membranes and sign of over-hydration will be assessed. Constant

observation of the patient will be done by study nurse. During the day investigators will be available in the ward. At night one of the investigators will be on call and be available in case need arises.

8. CLINICAL FAILURE AND INDICATIONS FOR DISCONTINUATION OF THE STUDY

a. Excessive vomiting - making the patient unable to drink;

b. Weight loss more than that on admission i.e. negative balance and appearance of severe dehydration;

c. Signs of electrolyte imbalance e.g. lethargy, restlessness etc;

d. Any patient continuing to pass watery stool more than 50 ml per kg per day longer than 5 days.

When all or any of the above signs are present, the investigator will re-examine the patient, take body weight, blood for serum electrolytes and specific gravity and the patient will be declared as therapeutic failure and referred for usual clinical care.

9. SPECIAL PROCEDURE FOR THE DIGESTIBILITY STUDY

For the digestibility study, 10 patients all aged less than one year will be included in each group of plantain-salt-solution, rice-salt-solution. Attempts will be made to admit only male patients of 1 month to 6 months who are not breast fed. This study will be carried out in the metabolic ward of ICDDR,B under close supervision of the specially trained nurses. In this group of children food will be withheld for the first 24 hours after admission but rehydration solution of the assigned variety will be fed according to the need as judged by the stool output and clinical condition. There is no danger in withholding food as the rehydration fluids are food-based and contain adequate calorie and other nutrients.

ICDDR,B is carrying out similar study without any problem. After the initial rehydration is accomplished a nonabsorbable marker (charcoal marker) will be fed to the child. This will be followed by rehydration solution. The time of appearance of the marker in the stool will be noted and will be marked as '0' hour. The interval between the feeding and the appearance of the marker will be taken as transit time. From the '0' hour up to 24 hour no food but only rehydration fluid will be given to the children. At the end of the 24 hour another marker will be fed to the patients. All samples of stool, urine and vomit from '0' hour until the appearance of the second marker will be collected and stored at -20°c. After the first 24 hours study is over, usual food will be allowed to the patients and oral rehydration therapy will be continued for up to five days or until soft stool appears. pH and osmolality of the catheter sample of the stool will be determined on admission and at 24 hours. Stool glucose pre- and post-hydrolysis will be measured from stool sample at '0' hour and from aliquotes of the collected stool between the two markers. Significant increase in the post hydrolysis glucose content along with increased osmolality and decreased pH will be considered as inadequate digestion of the starch from the food-based rehydration solution. Total calorie intake will be calculated from the rehydration fluid and calorie from the stool sample as determined by bomb calorimetry. Coefficient of absorption of calorie from all types of rehydration solution will be calculated by using the following formula: (16)

$$\frac{\text{Intake} - \text{output}}{\text{Intake}} \times 100$$

From the results calculations will be made for assessing the following aspects for all three types of rehydration solutions:

a. Per cent of absorption of calories and calorie balance;

b. Effect of therapy in terms of weight gain, output of stool, urine and vomiting, change in serum specific gravity and haematocrit;

c. Biochemical variables like serum- and stool electrolyte balance, and pre- and post hydrolysis glucose content of the stool;

d. Net stool output at 8 hour and 24 hour period;

e. Cumulative calorie balance for 24 hour periods until the end of the study.

It is recognised that the present method of estimation for carbohydrate absorption does not take into account the bacterial decomposition of undigested starch in the colon, but glucose content before and after hydrolysis together with measurement pH and osmolality will provide a fair estimation of carbohydrate absorption.

10. DATA ANALYSIS

Flow sheets for the study will be prepared and filled in for each patient to record 8 hourly intake, output, vital signs and body weight. Analysis of variance will be applied to establish overall significance between the three treatment groups. Individual group differences can be tested using Duncan's multiple range test.

In case ANOVA is not applicable 3 sample Median test or Kruskar-Wallis nonparametric test will be used.

D. SIGNIFICANCE

The results of this study will provide valuable information regarding the efficacy of rice-salt and plantain-salt solutions in the management of acute diarrhoea. If found successful, two very strong food-based

and inexpensive home-made oral rehydration solutions will be available. This will bring diarrhoea therapy to the doorstep of the mothers in the areas where rice and plantain are used as staple. Thus hopefully the use rate of ORT will go up which would reduce mortality from acute diarrhoea. Being based on food and having some extra calories and some not yet scientifically explained but obvious beneficial effects will help interrupting the diarrhoea malnutrition cycle. Besides this will reduce the gap between rehydration therapy, and dietary therpay, as the mother will use the same dietary ingredients for preparing rehydration fluid as well as the diet at the same time.

E. FACILITIES REQUIRED

i. No office space is required.

ii. Laboratory facilities for routine microbiology, biochemistry and clinical pathology are adequate.

iii. Hospital resources. The study will utilise patients selected from the treatment centre of ICDDR,B. The efficacy part will be carried out in the general study ward of the clinical research unit and the digestibility part will be conducted in the metabolic ward of ICDDR,B clinical research unit.

iv. Animal resources will be necessary for E. coli toxin assay.

v. Statistical data analysis — Help of the computer branch will be utilised. A personal computer will be adequate for this purpose and is being procured through another source.

TABLE I

COMPOSITION OF RIPE BANANA AND RICE POWDER PER 100 GRAM

Food	Protein	Fat	Mineral	Fibre Crude	Carbohydrate	Energy	Calcium	Phosphorus	Iron	Carotene	Thiamine	Riboflavin	Niacin	Vit. C	Potassium	Sodium
	g	g	g	g	g	kcal	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg
Ripe Banana	1.15	0.18	0.83	0.62	23.3	100	8.7	28	0.55	0.23	0.04	0.06	0.65	12	393	1.0
Rice powder	7.5	1.9	1.16	0.9	77.4	396	32	221	1.6	0.3	0.34	0.05	1.8	0	2.4	9

Davidson et al. 1979 (Ref. 13).

TABLE II

COMPOSITION OF 100 g OF PLANTAIN (COOKED AND MASHED) AS HAS BEEN ANALYSED IN ICDDR,B*

Protein g	Fats g	GLUCOSE		Total calorie kcal/100g	Potassium mmol/100g	Sodium mmol/100g	Chloride mmol/100g
		Pre-hydrolysis	Post-hydrolysis				
0.33	0.05	0.097 g	16.4 g	102	10.7	0	2.0

* L.T. Khan and A.M. Molla 1985 (unpublished).

TABLE III

COMPOSITION OF PROPOSED ORS IN ONE LITRE (1000 ml)

Food used (50g. rice equivalent)*		Electrolyte (mmol/l)	
		Na^+	K^+
Plantain-salt solution	200 g	90 mmol	20 mmol/l (indigenous source)
Rice-salt solution	50 g	90 mmol	
Water	1100 ml		

* Amount fixed on the basis of glucose content after in vitro hydrolysis.

TABLE IV

CRITERIA FOR SELECTION OF STUDY PATIENT

PARTICULARS	SELECTED	EXCLUDED
Age (months)	3 months - 59 months	Less than 3 months and greater than 59 months except in digestibility where 0-16 months will be selected.
History of diarrhoea	Upto two days	Greater than two days
Sex	Male	Female
H/O antibiotics	No antibiotic	Antibiotic
Blood count	Normal WBC	High count (greater than 15,000)
	Normal differential count	Shift to the left
Dehydration	Mild - moderate	Severe
Weight/Height	70 % of NCHS	<70 % of HCHS
Stool examination (M/E)		
Pus cells	Up to 20/HPF	Greater than 20

TABLE NO. V

CLINICAL COMPARIBILITY OF CHOLERA PATIENTS IN A PREVIOUS STUDY

VARIABLES	G-ORS N=21	R-ORS N=17
Age (years)		
Mean	47.4 ± 12.8	74.6 ± 11.6
Median	48	48
Range	30 - 72	30 - 60
Adm. weight	11.20 ± 2.0	11.50 ± 2.05
Dis. weight	12.14 ± 2.3	12.4 ± 2.3
Adm. Ser. specific gravity	1.0324 ± .0035	1.0313 ± .0044
Dur. diarrhoea	11.9 ± 7.0	11.4 ± 5.1
Dehydration status (%)		
Mild	0	0
Moderate	23.8	11.8
Severe	76.2	88.2

TABLE VI

DISTRIBUTION OF PATIENTS TO DIFFERENT FOOD-BASED ORS

Type of ORS	NO. OF PATIENTS
Plantain-salt solution	50 (40 + 10)
Rice-salt solution	50 (40 + 10)
Glucose-ORS	50 (40 + 10)
Total: three groups	150

TABLE VII

COMPARISON OF THE CLINICAL CHARACTERISTICS OF THE STUDY PATIENTS

(MEAN ± SEM)

VARIABLES	R-salt sol.	P-salt sol.	G-ORS	P value
Age (months)				
Mean				
Median				
Range				
Adm. weight				
Mean				
Median				
Adm. Hct				
Adm. Ser. Sp. Gr.				
Dur. illness (prior to adm.)				
Dehydration				
Mild n(%)				
Moderate n (%)				

TABLE VIII

BIOCHEMICAL VARIABLES OF STUDY PATIENTS TAKING DIFF. ORT

VARIABLES	Rice-salt soluion		Plantain-salt sol.		G - ORS	
	Adm.	24 hr	Adm.	24 hr	Adm..	24 hr
Na^+ (mmol/l)						
K^+ (mmol/l)						
Cl^- (mmol/l)						
TCO_2 (mmol/l)						

TABLE IX

TABLE TO COMPARE THE EFFICACY OF THE PLANTAIN-SALT AND RICE-SALT SOLUTIONS, AND STANDARD GLUCOSE ORS (MEAN ± SEM)

VARIABLES	Plantain-salt sol.	Rice-salt sol.	G - ORS
Stool output			
a. Total vol.(ml)			
1st 24 hour			
2nd 24 hour			
b. ml/kg day			
1st 24 hour			
2nd 24 hour			
Vomit			
a. Total vol. (ml)			
1st 24 hour			
2nd 24 hour			
b. ml /kg day			
1st 24 hour			
2nd 24 hour			
ORS intake			
a. Total vol. (ml)			
1st 24 hour			
2nd 24 hour			
b. ml/kg day			
1st 24 hour			
2nd 24 hour			

TABLE IX continued

VARIABLES	Plantain-salt sol.	Rice-salt sol.	G - ORS
Plain water intake			
a. Total volume (ml)			
1st 24 hour			
2nd 24 hour			
b. ml./kg/day			
1st 24 hour			
2nd 24 hour			
Combined intake (ORS + Water)			
a. Total volume (ml)			
1st 24 hour			
2nd 24 hour			
b. ml./kg.day			
1st 24 hour			
2nd 24 hour			
Urine output (ml)			
a. Total volume(ml)			
1st 24 hour			
2nd 24 hour			
b. ml./kg.day			
1st 24 hour			
2nd 24 hour			

TABLE IX continued

VARIABLES	Plantain-salt sol.	Rice-salt sol.	G - ORS
Gain in body weight (% of admission wt.)			
1st 24 hour			
2nd 24 hour			
Failure No (%)			

TABLE X

COMPARISON OF DIGESTIBILITY AND CALORIE BALANCE

VARIABLES	Plantain-salt sol.	Rice-salt sol.	G-ORS	P value
Stool pH				
'0' h.				
8 h.				
16 h.				
24 h				
Stool osmolality				
'0' h				
8 h				
16 h				
24 h				
Stool glucose(mmol/)				
Pre-hydrolysis				
'0' h.				
8 h.				
16 h				
24 h				
Post-hydrolysis				
'0' h				
8 h.				
16 h.				
24 h				

Table X continued

VARIABLES	Plantain-salt sol.	Rice-salt sol.	G - ORS	P value
Calorie balance				
24 hour				
48 hour				
72 hour				

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ABSTRACT SUMMARY FOR RESEARCH REVIEW COMMITTEE

1. A total of 150 children of age 1 month to 59 months will be studied as diarrhoea is a major problem in this age group.
2. There is no significant risk except blood for serum specific gravity, electrolytes and differential count will be done on admission for therapeutic purpose.
3. The study will be carried out in the study ward. Patients will be thoroughly examined physically before being entered into the study. Patients will remain under constant supervision of the experienced nurses. Investigators will be looking after the patients during the working hours and will be available in case of any need. Appropriate measures will be taken whenever any complication arises.
4. Confidentiality will be maintained by using hospital number of the patient during data analysis.
5. Informed consent form will be invariably obtained from the patients guardians after thorough discussion of the study procedure in Bengali.
6. The study does not involve any interview except relevant history of illness will be asked.
7. All patients will benefit from this study as well as the benefits will secure to the society with respect to the discovery of home-made solution from rice and plantain in prevention of dehydration and death from diarrhoea.
8. Hospital records and body fluid like stool, urine, vomitus and 3 ml of blood will be required on admission and at 24 hours.

SECTION III: BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES

Name	Annual salary	% of effort	PROJECT REQUIREMENTS Taka	US Dollars
1. Dr. A.M. Molla	US $65,000.00	15%		$ 9,750.00
2. Dr. Ayesha Molla	$20,500.00	15%		$ 3,075.00
3. Dr. Asma Khanam	Tk.185,000.00	20%	Tk.37,000.00	
4. Ms. Makhduma Khatun, Research Officer	Tk. 70,500.00	15%	10,575.00	
5. One Physician	Tk.125,000.00	25%	31,250.00	
6. Sr. Staff Nurse(4)	Tk. 97,100.00	25%	97,100.00	
7. One dietician	Tk.128,800.00	10%	12,900.00	
8. Study clerk	Tk. 42,000.00	10%	4,200.00	
9. Cleaners (4)	Tk. 60,000.00	10%	60,000.00	
			253,025.00 =	$ 9,036.00
		SUB-TOTAL :	US	$21,861.00

2. SUPPLIES AND MATERIALS:

Stationery	Tk.10,252.00	
Xeroxing and mimiographing	9,000.00	
Medical illustrations	6,000.00	
PUC bags		$ 650.00
ORS expenses	10,000.00	
	Tk.35,252.00 =	$ 1,259.00
SUB-TOTAL :		$ 1,909.00

3.	EQUIPMENT	None.	
4.	TRANSPORTATION OF PATIENTS AT THE END OF THE STUDY	Tk.15.00x1000 miles	Tk.15,000.00 = $ 537.00 SUB-TOTAL: $ 537.00

5. PATIENT HOSPITALIZATION:

(A) For efficacy studies

Rice-salt solution Plantain-salt solution G-ORS	40x5x3=600 pt. days Tk.200.00 per day x 600:	Tk.120,000.00

(B) For digestibility

3 x 10 = 30 patients x 5 day=150 days x 200 :	Tk. 30,000.00 Tk.150,000.00	= $5,357.00
	SUB-TOTAL :	$5,357.00

6. LABORATORY TESTS:

Blood test (TWBC, DC, Hct)	Tk.20x150=Tk.3000.00	
Stool microscopic exam.	Tk.10x150=Tk.1500.00	
Stool for culture	Tk.35x150=Tk.5250.00	
E. coli toxin assay(ST & LT)	Tk.30x150=Tk.4500.00	
ELISA for rotavirus	Tk.15x150=Tk.2250.00	Tk.16,500.00
BIOCHEMICAL TESTS:		
Pre and post hydrolysis glucose	Tk.75x150=Tk.11250.00	
Bomb calorimetry	Tk.150x30 =Tk. 4500.00	
Ser. electrolytes	Tk.70x350=Tk.24500.00	Tk.40,250.00
		Tk.56,750.00 = $ 2027.00
	SUB-TOTAL :	$ 2027.00

B. BUDGET SUMMARY

		US DOLLARS
1.	Personnel services	$ 21,861.00
2.	Supplies and materials	1,909.00
3.	Transportation of the patients	537.00
4.	Patient hospitalization	5,357.00
5.	Laboratory tests	2,027.00
	TOTAL :	$ 31,691.00

OVERHEAD WILL BE ADDED BY FINANCE

CONSENT FORM

Comparison of efficacy and digestibility of plantain-salt and rice-salt as home fluid with standard glucose ORS in the management of dehydration in acute diarrhoea in children.

International Centre for Diarrhoeal Disease Research is carrying out research to find out simple, effective and inexpensive treatment for diarrhoea. The presently available oral rehydration solution is one of the result of such research. Recently this centre has developed some new and improved type of oral rehydration solution which can be made from simple ingredients like cereal (rice) or plantain, available at home. Some of these simple rehydration solutions have been proved to be superior to the presently available oral rehydration solution. ICDDR,B would like to carry out further research in order to make more simplified diarrhoea treatment made from 50 g of rice and 5.3 g of salt or 200 g of plantain and 5.3 g of salt. Plantain-based ORS has the advantage of high content of potassium and a major staple food in many countries. We would request your permission for your child to participate in a trial in this hospital. This would involve taking the required amount of the rehydration solution for as long as your child continues to have liquid stool. In some cases food may be withheld from your child for the first 24 hours of treatment only and this will not cause any harm because the oral rehydration fluid as mentioned above will contain sufficient amount of calorie and other nutrients. All care will be taken so that your child does not suffer from any problem during the entire period. An amount of 3 ml of blood will be taken from your child on admission into the hospital and after 24 hours of treatment. The results of these blood test will be used to evaluate the efficacy of treatment. Your child will be allowed to go home after his/her diarrhoea has stopped. You are completely

free to choose not to participate in this research and in any case your child will be provided with appropriate treatment of diarrhoea as available in ICDDR,B.

Finger print/Signature of
the patient/guardian _____

Signature of the
Investigator _____

Date_____

অনুমতি পত্র

কাঁচকলা ও লবন দ্বারা ঘরে তৈরী গ্লুকোজ স্যালাইনের পুষ্টিমানসহ কার্যকারিতা এবং পাচন যোগ্যতা নির্নয় গবেষনা।

আন্তর্জাতিক উদরাময় গবেষনা কেন্দ্র ডাইরিয়া রোগ নিরাময়ের জন্য কার্যকরী ও সুলভ চিকিৎসা পদ্ধতি উদ্ভাবনের গবেষনা করছে। বর্তমানের ব্যবহৃত মুখে খাবার স্যালাইন ঐরকম গবেষনার ফল। সম্প্রতি এ কেন্দ্র আরও উন্নত ধরনের মুখে খাবার স্যালাইন উদ্ভাবন করেছে যা ঘরে ব্যবহৃত সাধারন খাদ্যদ্রব্য যেমন চাউল, কাঁচকলা ইত্যাদি দিয়ে তৈরী করা হয়। এগুলির কোন কোনটি আগের স্যালাইনের চেয়ে অধিক কার্যকর বলে প্রমানিত হয়েছে। এ কেন্দ্র ডাইরিয়ার চিকিৎসার জন্য আরো সহজ ব্যবস্থা হিসাবে ৫০ গ্রাম চাউল ও ৫০ গ্রাম লবন অথবা ২০০ গ্রাম কাঁচকলা ও সমপরিমান লবন একত্রে নতুন মুখে খাবার স্যালাইনের গবেষনায় উদ্যোগী হয়েছে। কাঁচকলা দ্বারা প্রস্তুত স্যালাইনে অধিক পরিমানে পটাশিয়াম লবন থাকায় এবং অনেক দেশে প্রধান খাদ্য হিসাবে কাঁচকলার ব্যবহার এর অন্যতম সুবিধা। আমরা এ গবেষনায় আপনার সন্তানের উপর প্রয়োগের অনুমতি প্রার্থনা করি। সন্তান পাতলা পায়খানা চলতে থাকে ততক্ষন পর্যন্ত রোগীকে মুখে খাবার এ নতুন স্যালাইন পরিমানমত খেতে হবে। কোন কোন ক্ষেত্রে চিকিৎসা চলাকালীন প্রথম ২৪ ঘন্টা রোগীকে অন্য কোন খাবার খেতে দেয়া হবে না। তবে এতে রোগীর কোন ক্ষতি হবে না। কেননা উপরোক্ত খাবার স্যালাইনে যথেষ্ট পরিমান পুষ্টিকর পদার্থ আছে। চিকিৎসা চলাকালীন সময়ে আপনার সন্তানের যাতে অন্য কোন অসুবিধা না হয় তার প্রয়োজনীয় ব্যবস্থা নেয়া হবে। রোগীর ভর্তির সময় এবং ২৪ ঘন্টা পর প্রতিবারে অল্প পরিমান রক্ত (১ মিঃ লিঃ) পরীক্ষার জন্য নেয়া হবে। এর মাধ্যমে প্রস্তাবিত এ চিকিৎসার কার্যকারিতা নির্নয়ের

জন্য ব্যবহৃত হবে। পাতলা পায়খানা ভালো হলে আপনার সন্তানকে বাড়ী যেতে দেওয়া হবে। এ গবেষণায় অংশ গ্রহণে আপনার কোন বাধ্যবাধকতা নেই। অংশ গ্রহণ না করলেও আপনার সন্তান এ হাসপাতালের প্রচলিত নিয়মে সুচিকিৎসা পাবে।

- - - - - - - - - - - - - -
রোগীর বা অভিভাবকের স্বাক্ষর
বা টিপসহি

তারিখ - - - - - - -

- - - - - - - - - - - - - -
ডাক্তারের স্বাক্ষর

ANNEXURE 1

Patient's name _____

FORM NO. 1

Hos. No. _____

Plantain based ORS study

Date of adm. _____

Type of sol. _____

Date, time & hours	Patient's weight	I.V. in ml	Plain H_2O in ml	ORS in ml	OUTPUT			
					Stool	Urine	Vomitus	Type of stool
Admission								
8/80 h								
16/88 h								
24/96 h								
32/104 h								
40/112 h								
48/120 h								
56/128 h								
64/136 h								
72/144 h								

Form No. 2

Annex. 2

Adm. No._____

Plantain based ORS study

Weight _____

Height _____

Name of the patient_____ Age _____ Sex _____ Duration of diarrhoea prior to Adm.(h)_____

Hours (time)	Pulse/ minute	Res/ minute	Skin turgor *	Tongue **	Dehydration ***	Blood pressure	Temperature
Admn. 0 h							
8 h							
16 h							
24 h							
32 h							
40 h							
48 h							
56 h							
64 h							

* 0 = Normal, 1 = Fair, 2 = Poor

** 1 = Moist, 2 = Dry, 3 = Very dry

*** 1 = Mild, 2 = Moderate, 3 = Mod. to sev., 4 = Severe

Annex. 3

FORM NO. 3

LABORATORY INFORMATION SHEET

Patient No. _____

Plantain based ORS study

Date of Adm. _____

Time	Serum Sp. gravity	Hct	Blood electrolytes					Stool electrolytes				Urine electrolytes			Vomitus electrolytes		
			Na^+	K^+	Cl^-	TCO_2^-	Glucose	Na^+	K^+	Cl^-	pH	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-
Admn. 0 h																	
24 h																	
48 h																	
Failure																	